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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,647	04/03/2006	Franck Chaubron	CAM-33610	6698

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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
11/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,647	CHAUBRON ET AL.	
	Examiner	Art Unit	
	DAVID C. THOMAS	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11,13 and 15-27* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 20-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,8-11,13 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/29/2007; 11/3/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-19, 28 and 29, in the reply filed on September 25, 2008 is acknowledged. Applicant also elected SEQ ID NOS: 1, 2 and 11 representing a forward and reverse primer and a forward probe, respectively. Claims 4-7 are withdrawn since these claims are drawn to non-elected SEQ IDS. Claims 20-27 are also withdrawn since these claims are drawn to non-elected subject matter (kit). Applicant's amendment of claims 1, 11 and 15-18, in the reply filed on 24 October 2008 is also acknowledged. Claims 2, 12, 14, 28 and 29 have been newly canceled. Therefore, claims 1, 3-11, 13 and 15-27 are currently pending and claims 1, 3, 8-11, 13, and 15-19 will be examined on the merits.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3, 8-11, 13, and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rothman et al. (U.S. Patent No. 6,699,670) in view of Legerski, R.J. (U.S. Patent No. 6,406,891).

With regard to claims 1, 10 and 13, Rothman teaches a method for determining the presence of living bacteria or fungus-yeast in a sample by detecting DNA that comprises a selected target region of ribosomal RNA (rRNA) genes (for overview, see Abstract and column 2, lines 17-42), said method comprising:

(a) extracting deoxyribonucleic acid (DNA) from said sample (fifteen common microorganisms were cultured, including mostly eubacteria, and DNA was extracted using the QIAamp DNA kit, column 6, lines 51-64; clinical samples are obtained from patients suspected of having bacteremia, column 6, lines 1-8);

(c) incubating said DNA from said sample with a thermostable enzyme with DNA-dependent Polymerase activity and polynucleotide primers that hybridize to the selected rRNA gene target region of bacteria or fungus-yeast but not of other organisms (primers were designed to amplify a segment of virtually any eubacterial 16S rRNA in the presence of that eubacterial template, column 4, line 63 to column 5, line 5), under conditions which allow the said DNA polymerase activity to amplify said DNA to a detectable level by Polymerase Chain Reaction (PCR reactions are performed using a sequence detection system, column 8, lines 1-17) and;

(d) detecting the amplified cDNAs from said rRNA target region by hybridization with one or more probe polynucleotide(s) that hybridizes to said amplified cDNAs of bacteria or fungus-yeast but not other organisms, wherein step (c) and (d) are performed in the same tube by means of one step real-time PCR (real-time PCR is performed using fluorogenic probes that bind to amplified template molecules and are degraded during amplification by the DNA polymerase, column 4, lines 54-62; the probes hybridize to either conserved or divergent regions of eubacteria, column 5, lines 28-41).

With regard to claims 3, 8, and 15-17, Rothman teaches a method wherein the polynucleotide primers and probe consist of the sequences (see Table 1 for listing of primer and probes for universal detection of eubacterial rRNA gene sequences):

Seq ID No 1 TGGAGCATGTGGTTTAATTCGA [primer forward] (identical in length and sequence to SEQ ID No 1 of Rothman);

Seq ID No 2 TGCGGGACTTAACCCAACA [primer reverse] (identical in length and sequence to SEQ ID No 2 of Rothman)

Seq ID No 11 TGCATGGYTGTCGTCAGCTCGTG [probe forward] (identical in length and sequence to SEQ ID No 7 of Rothman; SEQ ID No 3 of Rothman, shown in Table 1, is the reverse complement of Seq ID No 11).

With regard to claim 9, Rothman teaches a method wherein the polynucleotide primers and probes are natural nucleic acid or Peptide Nucleic Acid (PNA) which can hybridize to nucleic acid (DNA and RNA) (primers and probes are designed for optimized melting temperatures, secondary structure, base composition and amplicon

lengths for optimized primer binding and detection by probe hybridization to amplified eubacterial 16S rRNA gene sequences, column 7, lines 41-67).

With regard to claim 10, Rothman teaches a method further comprising the step of quantifying the RNA by comparison with a quantified external standard DNA from the group consisting of: *Escherichia coli* and *Candida spp* (amplification of DNA target sequences from eubacteria were compared to a control target of *Candida albicans*, column 9, line 42 to column 10, line 4).

With regard to claims 18 and 19, Rothman teaches a method wherein the polynucleotide probes further comprise a non-radioactive label such as fluoroscein (dual-labeled hybridization probes contain a quencher dye at the 3' end and either VIC or FAM at the 5' end, column 7, lines 50-63).

Rothman does not teach a method for determining the presence of bacteria in a sample by detecting RNA that comprises a selected region of rRNA, including treatment of extracted RNA samples with DNase and using a thermostable enzyme such as Tth DNA polymerase with both reverse transcriptase and DNA polymerase activities to first synthesize cDNA from the rRNA and then amplify the cDNA in a one-step real-time RT-PCR. Rothman also does not teach a method further comprising the step of quantifying the RNA by comparison with a quantified external standard RNA from the group consisting of: *Escherichia coli* and *Candida spp*.

Legerski teaches a method of producing cDNA in a one-step RT-PCR procedure using enzymes such as Retrotherm RT, RetroAmp RT DNA polymerase and Tth DNA polymerase that synthesize a first strand cDNA at elevated temperatures followed by cycling to amplify the cDNA in a PCR step (column 9, lines 15-21 and 54-59, column 10, lines 5-23 and column 11, lines 14-25). Legerski teaches the use of RetroAmp RT DNA polymerase to prepare cDNA from rRNA sequences of *E. coli* (column 10, lines 23-35). Legerski also teaches a method of preparation of RNA that includes treatment of the extracted RNA with DNase I prior to the RT-PCR step (column 23, line 60 to column 24, line 2 and column 24, lines 52-60).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the real-time PCR method for detection of eubacteria taught by Rothman based on amplification of segments of rRNA genes containing both conserved and divergent sequences and the method taught by Legerski for preparation of cDNA sequences using a one-step RT-PCR procedure since both references teach amplification of sequences representing the highly conserved 16S rRNA genes of bacteria. Thus, an ordinary practitioner would have been motivated to apply the one-step RT-PCR procedure of Legerski to the real-time detection method of eubacteria using the primers and probes of Rothman. Rothman teaches that a method using a select set of primers and probes that detect virtually any eubacterial 16S rRNA gene sequence if that organism is present in the sample (column 5, lines 6-8, Figure 5 and Table 1). Legerski teaches that using thermostable reverse transcriptases allows

the first-strand cDNA synthesis step to be performed at an elevated temperature, minimizing the effect of RNA secondary structure, and enables synthesis of both strands in a single tube with no buffer changes (column 9, lines 15-21 and 54-59). Legerski states "when primers are available for both strands, single-tube synthesis with Retrotherm RT is easy, fast and powerful, even when working with mixed populations of RNA" (column 9, lines 31-34).

Conclusion

5. Claims 1, 3, 8-11, 13, and 15-19 are rejected. No claims are allowable.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

/David C Thomas/
Examiner, Art Unit 1637

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637